Brain Arteriovenous Malformations and Endovascular Treatment: Effect on Seizures

X. LV, Y. LI, C. JIANG, X. YANG, Z. WU

Beijing Neurosurgical Institute, Beijing Tiantan Hospital, Capital Medical University; Beijing, China

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Summary

We report our experience in treating patients with seizures associated with brain arteriovenous malformations (AVM) without a clinical history of intracranial hemorrhage.

Between 2001 and 2003, the neurovascular unit at Beijing Tiantan Hospital treated 109 patients with brain AVM endovascularly. Thirty patients (27.5%) experienced seizures before treatment. We studied the following factors: sex, age, AVM size, AVM location, seizure type, duration of seizure history, endovascular treatment and AVM obliteration. Clinical follow-up was via telephone interview.

Thirty patients with seizure disorders due to brain AVMs were endovascularly treated. The age of the patients ranged from eight to 55 years. There were 22 males and eight females. The AVMs were smaller than 3 cm in five patients, between 3 cm and 6 cm in 22, and larger than 6 cm in three. The most frequent location of the AVMs was in the frontal, followed by the parietal, temporal and occipital lobes. Sixty-seven embolization procedures were performed and total obliteration was achieved in four patients. Two patients developed a hemiparesis and three suffered temporary dysphasia after embolization. Two patients had visual field deficits. There were no deaths. The results of post-embolization seizure control during the average follow-up period of 80 months were excellent in 21 patients, good in four, fair in two and poor in three. Successful seizure control can be obtained with endovascular embolization.

Introduction

Seizure is the second most frequent clinical presentation of brain AVMs following hemorrhage, with 30% of all patients presenting with generalized seizures and 10% presenting with focal seizures [1]. Previous reports of seizure outcomes after brain AVM treatment have primarily involved surgery and radiosurgery. The results of surgical treatment for seizure control were successful in some reports [2,3] and radiosurgery can improve seizure outcomes in majority of patients [4]. However, patients who did not experience seizures before treatment may exhibit new-onset seizures after surgery and radiosurgery. There are relatively few reports of seizure results after AVM embolization [3], partly because embolization is primarily used as an adjunct to surgery or radiosurgery. We report the seizure results after endovascular embolization of brain AVMs.

Patients and Methods

Between January 2001 and January 2003, the neurovascular unit at Beijing Tiantan Hospital treated 109 consecutive patients with brain AVMs endovascularly. Thirty patients (27.5%) had seizure disorders and brain AVMs with no history of cerebral hemorrhage before treatment. All of these patients had been treated medically and were consider disabled due to failure or side-effects of anticonvulsant therapy or the effect upon their professional lives of even infrequent seizures.

Clinical Presentation

The patients included 22 males and eight females with mean age 31 years (range eight to 55 years). Seventeen patients had generalized seizures without aura or focal symptoms, six had simple partial seizures, one had complex partial seizures, and six had partial seizures with secondary generalization. The duration of seizure history varied from one month to 20 years, with an average of five years. The findings on neurological examination included progressive mental changes in three patients, and limb palsy in two. One patient had a right homonymous hemianopsia (Table 1). All AVMs were supratentorial, 20 lesions were in the right hemisphere and 15 in the left hemisphere. The most frequent location was in the frontal lobe, followed by the parietal, temporal and occipital lobes. There were five small, 22 medium, and three large lesions in this group (Table 2).

The size of the AVMs was characterized as small if it measured less than 3 cm in diameter, medium if it measured between 3 cm and 6 cm in diameter, and large if it measured more than 6 cm in diameter. For the purpose of the follow-up analysis of seizure control, outcome was classified as excellent if the patient became seizure-free or experienced no more than an occasional aura, good if the patient had a 90% reduction in seizure frequency, fair if the patient had a 50% reduction in seizure frequency, and poor if there was less than a 50% reduction in the frequency of seizures. The follow-up period of these patients ranged from 24 to 96 months (average 80 months). All patients continued receiving anticonvulsant therapy for one year after embolization of the lesion. Anticonvulsant drugs were discontinued as patients became seizure-free.

Embolization

After the induction of neuroleptic anesthesia, a 5F or 6F guiding catheter was positioned in the high cervical internal carotid artery or vertebral artery. Systemic anticoagulation was achieved using 4000 to 5000 units of heparin. Microcatheters of variable stiffness (Prowler10, Cordis Endovascular Systems, Miami, FL, USA) or flow-directed microcatheters (Magic-1.2F, Balt, France; Marathon, M.T.I-ev3) were used for selective vessel catheterization and embolization. When embolization was considered safe, 5-0 silk suture cut into 0.5-1 cm lengths microcoils, NBCA or Onyx18 as the sole or combined embolic agent. Intermittent fluoroscopy was used to assess the catheter position and the rate of blood flow through the pedicle being embolized. The other embolization session of would be performed over a period of weeks to months.

Results

Embolization Results

Silk and detachable coils was the sole embolic agent used in 11 patients(36.7%). NBCA was the sole embolic agent used in ten patients (33.3%). Silk, coils and NBCA were combined in five patients (16.7%). Silk, coils, NBCA and Onyx 18 were combined in remaining four patients (13.3%). Total obliteration of AVM was achieved in four patients (13.3%). None of the 30 patients who underwent endovascular treatment for seizures associated with brain AVMs died postoperatively. One AVM ruptured during embolization, four patients developed transient neurological deficits after embolization and two patients suffered AVM rupture during follow-up at three and six years respectively.

Seizure Results

The results of seizure control in a limited follow-up period were excellent in 21 patients, good in four, fair in two, and poor in three. Four patients with small AVMs underwent complete emblization with an excellent result. Eighteen patients became seizure-free after one embolization, two became seizure-free after a second embolization and one became seizure-free after a third embolization.

Discussion

In an international multicenter study of 1289 patients with brain AVMs, seizures were second to intracranial hemorrhage as the most common presentation, with 30% of all patients presenting with generalized seizures and 10% presenting with focal seizures [1].

The incidence of patients with AVMs presenting with seizures and with no clinical evidence of intracranial hemorrhage varies between 17% and 40% [5]. Thirty (27.5%) of 109 patients with brain AVMs in our series experienced seizures before treatment. Most experienced generalized tonic clonic seizures (56.7%), whereas others experienced simple partial (20%), complex partial (3.3%) seizures,

or partial seizures with secondary generalization (20%). Seizure pattern seemed related to the location of the AVMs in this series. Most parietal lobe AVMs presented with secondary generalization, frontal and temporal lobe AVMs were associated with generalized seizures, and parietotemporal lobe AVMs presented with simple partial seizures. Reports suggest that larger AVMs with superficial components are more likely to be complicated by epilepsy than by hemorrhage [6]. Turjman et Al [7] analyzed the angioarchitectural characteristics of AVMs for an association with seizure incidence and observed that cortical locations, feeding by the middle cerebral artery, an absence of aneurysms, cortical locations of the feeders, the presence of varices, and an absence of intranidal aneurysms were significantly associated with seizures [7]. On the other hand, superficial venous drainage was not found to be associated with seizures [8]. The presence of varices in the venous drainage was found to be predictive of epilepsy. This factor is predictive only when considered among other factors.

When considered alone, the presence of varices was not found to correlate statistically with epilepsy. Several groups have reported an association between larger AVM sizes and greater incidences of seizures [6,9,10]. Of the 27 patients in Yeh et Al series, 18 had AVMs that were 4 cm or greater in size [5]. The larger AVMs tended to have more arteriovenous shunting of blood, a factor that is associated with focal cerebral ischemia. Although none of the patients in their study had a history suggestive of intracranial hemorrhage, specimens in ten patients contained hemosiderin deposits suggesting the probability of an unrecognized or subclinical intracranial hemorrhage.

Hoh et Al found that male sex, age of less than 65 years, AVM size of more than 3 cm, and temporal lobe AVM location to be statistically associated with pretreatment seizures [8]. These features may act as therapeutic targets for either surgery or embolization. Knowledge of these specific factors may also help provide a morphological basis for the persistence of epilepsy after AVM treatment. This identification could help in understanding the failure to eliminate the symptom of epilepsy after AVM treatment.

The cause of epileptogenesis from cerebral AVMs is still unclear [8]. It is our opinion that the principal mechanism of seizure in patients with AVMs is focal cerebral ischemia as a result of arteriovenous shunting and gliosis of the surrounding brain tissue with secondary epileptogenesis, especially in the temporal lobe. Heikkinen et Al. reported that seven out of 27 AVM patients who had no history of hemorrhage exhibited focal hemosiderin deposits; only two of these had other histological evidence of previous hemorrhage [11].

The decision to treat epileptogenic, unruptured AVMs is still a subject of controversy [12,13]. In 1984, Fults and Kelly reviewed their series of 83 nonsurgically managed patients with an average follow-up period of eight years; 26 patients presented with seizures, seven (26.9%) of whom suffered a hemorrhage. The condition of 18 patients was described as good, but seizure control was not reported [14]. Epilepsy as an indication for surgical treatment of AVMs has been questioned in the literature [15], since the results of surgery have been reported differently. Parkinson and Bachers reported surgery for 100 patients with cerebral AVMs, 28 of whom presented with a seizure disorder [16]. Only one patient became seizure-free after surgery. Moreover, 8% of the patients who had no epilepsy before surgery developed seizures some time later.

Forster et Al reported 150 patients treated surgically for AVMs of the brain, with an average follow-up period of over 15 years. Only 14% of patients who had previously suffered from epilepsy showed a reduction of seizure frequency or became easier to control after surgery, while 22% not previously epileptic developed seizures after surgery. According to a report by Crawford et Al [6] on 75 patients who underwent total AVM excision, 20 years after surgery there was a 57% risk of developing epilepsy among surgically treated patients. Patients aged ten to 19 years at the time of diagnosis faced an 82% risk of developing seizures 20 years after surgery [6]. Yeh et Al operated on 27 patients with epilepsy; in 21 the seizures were eliminated.

They concluded that excision of an AVM alone would not relieve seizure disorders unless the epileptogenic focus was removed during excision of the AVMs [5]. In more recent studies, however, results of seizure outcomes after radiosurgery significantly improved and are now reported between 62% [17] and 80% [18]. However, new-onset seizures can be a complication of radiosurgery. In a multicenter analysis of

Table1 **Patients presented with seizures associated with brain AVMs.**

Pat. No.	Age/ sex	Duration (yrs)	Type	Site (cm)	Size	Treatment	Complications	Seizure control	Follow-up (Months)
1	29/M	17	GT	lf, occipital	4	1, suture/coil 2, suture/coil	None	Excellent	72
2	39/M	3	GT	lf, temporal	3	1, suture/coil 2, NBCA	None	Excellent	94
3	55/M	20	PG	rt, frontotemporal	7	1, suture/coil	Rupture lf, hemiparesis	Excellent	96
4	37/M	7	PG	lf, frontotemporal	5	1, suture/coil 2, NBCA	None	Good	36
5	14/F	1/2	PG	lf, temporoparietal	5	1, suture/coil 2, NBCA 3, NBCA 4, NBCA	None	Poor	72
6	38/M	3	SP	rt, parietal	2	1, NBCA 2, suture/coil 3, suture/coil 4, suture/coil	None	Poor	88
7	21/M	5	SP	rt, temporoparietal	6	1, suture/coil 2, NBCA 3, NBCA 4, ONYX	Transient left leg palsy rupture after 3 yrs	Excellent	92
8	34/M	2	PG	rt, parietal	2	1, suture/coil 2, suture/coil 3, suture/coil 4, suture/coil	None	Fair	90
9	26/F	15	GT	lf, frontal	4	1, suture/coil	None	Excellent	93
10	30/M	1	GT	lf, frontal	2	1, suture/coil	None	Excellent	86
11	37/M	20	GT	lf, frontal	3	1, suture./coil 2, suture/coil	Transient aphasia	Excellent	88
12	13/M	1/4	SP	rt, temporal	2	1, suture/coil complete	None	Excellent	96
13	28/M	8	GT	lf, parietal	3	1, suture/coil	Transient right hemiparesis	Excellent	94
14	28/F	1/10	GT	lf, parietal	3	1, NBCA	None	Excellent	80
15	26/M	8	GT	lf, temporal	4	1, suture/coil	None	Excellent	96
16	8/M	2	GT	lf, frontal	5	1, suture/coil	None	Excellent	79
17	38/F	8	SP	rt, frontal	7	1, suture/coil 2, NBCA 3, NBCA 4, ONYX	Transient left leg palsy rupture after 6 yrs	Excellent	24
18	32/M	1/12	GT	lf, temporal	5	1, NBCA 2, suture/coil 3, suture/coil 4, ONYX	None	Excellent	60
19	20/F	1/12	PG	Lf, parietal	4	1, NBCA 2, NBCA	None	Excellent	79

Pat. No.	Age/ sex	Duration (yrs)	Type	Site (cm)	Size	Treatment	Complications	Seizure control	Follow-up (Months)
20	48/M	1/12	GT	rt, temporal	4	1, NBCA 2, NBCA 3, NBCA	None	Excellent	96
21	29/M	7/12	SP	rt, frontal	3	1, suture/coil	None	Excellent	71
22	18/F	1/2	GT	rt, parietal	7	1, suture/coil 2, NBCA	None	Excellent	89
23	37/M	12	SP	lf, temporoparietal	5	1, NBCA	None	Poor	95
24	39/F	4	GT	lf, temporal	4	1, NBCA	None	Excellent	94
25	31/M	1/12	SP	lt, temporoparietal	4	1, NBCA 2, NBCA	None	Excellent	84
26	36/M	1/4	GT	rt, temporal	5	1, NBCA 2, NBCA 3, NBCA	None	Fair	77
27	41/F	7	GT	rt, frontoparietal	6	1, NBCA 2, NBCA	None	Good	79
28	42/M	1/12	GT	rt, frontal	4	1, coil 2, NBCA 3, ONYX	None	Good	54
29	31/M	4	GT	rt, frontal	5	1, NBCA 2, NBCA 3, NBCA 4, NBCA	None	Excellent	59
30	24/M	1	PG	rt, parietal	6	1, NBCA 2, NBCA 3, NBCA	None	Good	77

M, male; F, female; GT, generalized tonicoclonic; PG, primary generalized; SP, simple partial.

Table 2 **Locations and seizure types.**

Locations	No.	Partial			Generalized Tonicoclonic
		Simple	Complex	With secondary generalization	
Frontal	8	2	0	0	6
Parietal	7	1	0	3	3
Temporal	7	1	0	0	6
Occipital	1	0	0	0	1
Frontoparietal	1	0	0	0	1
Frontotemporal	2	0	0	2	0
Parietotemporal	4	2	1	1	0
Total	30	6	1	6	17

complications of radiosurgical AVM treatment, 22 out of 1255 patients (1.8%) experienced new or worsened seizures [13]. Some authors think that radiosurgery has beneficial effects on seizure outcomes even before complete AVM obliteration [9,11,19-23], although higher seizure-free rates were observed for patients with complete obliteration [9,21,22]. One possible explanation is that irradiation might affect epileptogenesis from tissue surrounding the AVM, independent of radiation-induced AVM thrombosis[11,19,20,24-26]. Others think that radiosurgical reduction of the steal phenomenon contributes to the resolution of epileptogenic activity from surrounding ischemic areas [11,19,22]. Hoh et Al. achieved excellent seizure results by using a multimodality treatment (neurosurgery, radiosurgery or embolization) approach for AVMs in more than 70% patients with 5.7% new-onset seizures after AVM treatment [8].

There are relatively few reports of seizure results after AVM embolization [3], partly because embolization is primarily used as an adjunct to surgery or radiosurgery. If AVM epileptogenesis is indeed attributable to a steal phenomenon, then it is conceivable that embolization would have a beneficial effect on seizure control. Our results of 30 patients who had cerebral AVMs with a mean follow-up period of 80 years; 70% achieved complete elimination of seizures after endovascular embolization. Secondary foci may account for failure of treatment to eliminate the seizure. This phenomenon is likely to occur in about 20% of patients [5]. It corresponds to epileptic foci distant from the primary AVM, usually located in the ipsilateral mesial temporal region [27].

In previous surgical series, factors associated with better postoperative seizure control were shorter seizure duration before AVM treatment [28], no history of hemorrhage [6], and older patient age [6,28]. Factors associated with better seizure outcomes in radiosurgical series were shorter duration of epilepsy before treatment [22,29], small AVM size [29], older patient age [29], AVM locations on central structures or in the parietal area [11], and no history of hemorrhage [21]. In a wider spectrum of brain AVMs treated via a multidisciplinary approach, Hoh et Al [8] observed the following factors to be associated with good seizure outcomes: short seizure history, association of seizures with intracranial hemorrhage, generalized tonicoclonic seizure type, deep and posterior fossa AVM locations, surgical resection, and complete AVM obliteration. When only completely obliterated AVMs were considered, there were no statistically significant differences between surgery, radiosurgery, and embolization with respect to seizure control. The association between AVM obliteration and seizure outcome is debatable [4].

There are potential limitations in the present study that need to be considered. The relatively small sample size and variable duration of seizures before treatment also make determination of the significance of predictive factors more difficult. Although preoperative EEG evaluation (with conventional scalp EEG recording) is valuable in the localization of an epileptiform focus, EEG is usually not considered in our patients because EEG usually shows a non-specific lateralized slow wave focus on the EEG (without well-defined sharp waves and spike activity) in cases of AVMs [30].

Conclusions

In this small series, endovascular treatment for brain AVMs achieved excellent seizure control results.

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Zhongxue Wu
Beijing Neurosurgical Institute
No.6, Tiantan Xili, Chongwen
Beijing, 100050
P.R.China
E-mail: ttyyzjb@sina.com
lvxianli000@163.com